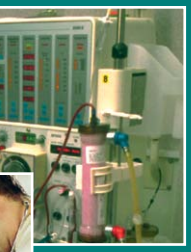


Childhood Nephrotic Syndrome

What is childhood nephrotic syndrome?

Childhood nephrotic syndrome is not a disease in itself; rather, it is a group of symptoms that

- indicate kidney damage—particularly damage to the glomeruli, the tiny units within the kidney where blood is filtered
- result in the release of too much protein from the body into the urine

When the kidneys are damaged, the protein albumin, normally found in the blood, will leak into the urine. Proteins are large, complex molecules that perform a number of important functions in the body.

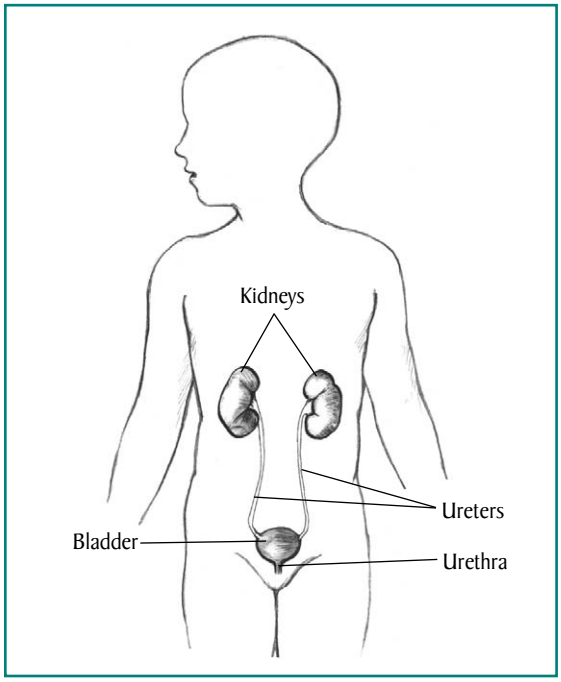
The two types of childhood nephrotic syndrome are

- primary—the most common type of childhood nephrotic syndrome, which begins in the kidneys and affects only the kidneys
- secondary—the syndrome is caused by other diseases

A health care provider may refer a child with nephrotic syndrome to a nephrologist—a doctor who specializes in treating kidney disease. A child should see a pediatric nephrologist, who has special training to take care of kidney problems in children, if possible. However, in many parts of the country, pediatric nephrologists are in short supply, so the child may need to travel. If traveling is not possible, some nephrologists who treat adults can also treat children.

What are the kidneys and what do they do?

The kidneys are two bean-shaped organs, each about the size of a fist. They are located just below the rib cage, one on each side of the spine. Every day, the kidneys filter about 120 to 150 quarts of blood to produce about 1 to 2 quarts of urine, composed of wastes and extra fluid. Children produce less urine than adults and the amount produced depends on their age. The urine flows from the kidneys to the bladder through tubes called ureters. The bladder stores urine. When the bladder empties, urine flows out of the body through a tube called the urethra, located at the bottom of the bladder.

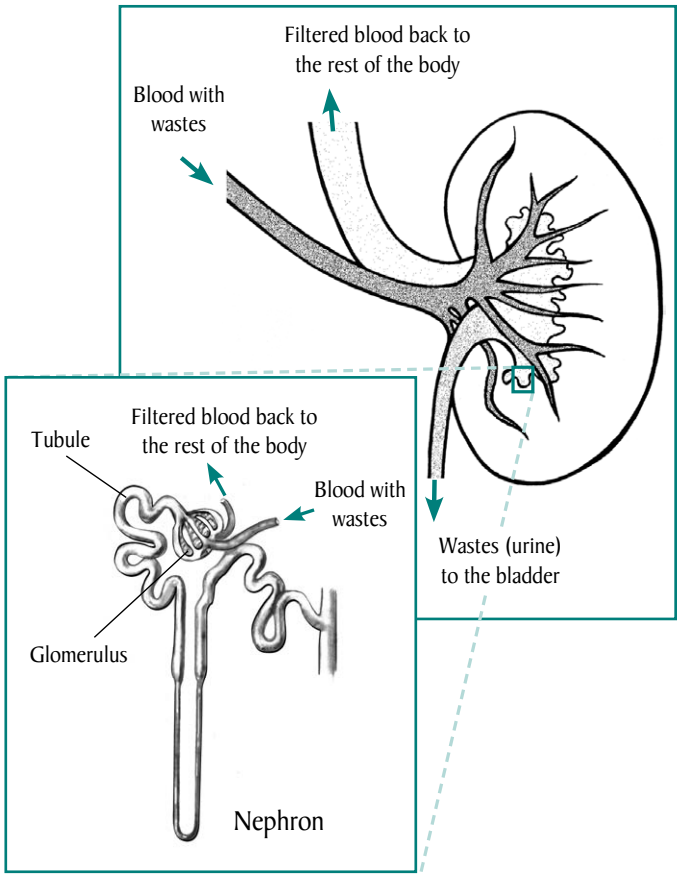


The urine flows from the kidneys to the bladder through tubes called ureters.

National Institute of Diabetes and Digestive and Kidney Diseases

National Kidney and Urologic Diseases Information Clearinghouse

Kidneys work at the microscopic level. The kidney is not one large filter. Each kidney is made up of about a million filtering units called nephrons. Each nephron filters a small amount of blood. The nephron includes a filter, called the glomerulus, and a tube. The nephrons work through a two-step process. The glomerulus lets fluid and waste products pass through it; however, it prevents blood cells and large molecules, mostly proteins, from passing. The filtered fluid then passes through the tubule, which sends needed minerals back to the bloodstream and removes wastes.



Each kidney is made up of about a million filtering units called nephrons. Each nephron filters a small amount of blood. The nephron includes a filter, called the glomerulus, and a tubule.

What causes childhood nephrotic syndrome?

While idiopathic, or unknown, diseases are the most common cause of primary childhood nephrotic syndrome, researchers have linked certain diseases and some specific genetic changes that damage the kidneys with primary childhood nephrotic syndrome.

The cause of secondary childhood nephrotic syndrome is an underlying disease or infection. Called a primary illness, it's this underlying disease or infection that causes changes in the kidney function that can result in secondary childhood nephrotic syndrome.

Congenital diseases—diseases that are present at birth—can also cause childhood nephrotic syndrome.

Primary Childhood Nephrotic Syndrome

The following diseases are different types of idiopathic childhood nephrotic syndrome:

- **Minimal change disease** involves damage to the glomeruli that can be seen only with an electron microscope. This type of microscope shows tiny details better than any other microscope. Scientists do not know the exact cause of minimal change disease.

  Minimal change disease is the most common cause of idiopathic childhood nephrotic syndrome.[1]

- **Focal segmental glomerulosclerosis** is scarring in scattered regions of the kidney:
  - "Focal" means that only some of the glomeruli become scarred.
  - "Segmental" means damage affects only part of an individual glomerulus.

[1]Nephrotic syndrome. The Merck Manuals Online Medical Library. www.merckmanuals.com/home/kidney_and_urinary_tract_disorders/kidney_filtering_disorders/nephrotic_syndrome.html. Updated July 2013. Accessed July 7, 2014.

- **Membranoproliferative glomerulonephritis** is a group of disorders involving deposits of antibodies that build up in the glomeruli, causing thickening and damage. Antibodies are proteins made by the immune system to protect the body from foreign substances such as bacteria or viruses.

Secondary Childhood Nephrotic Syndrome

Some common diseases that can cause secondary childhood nephrotic syndrome include

- diabetes, a condition that occurs when the body cannot use glucose—a type of sugar—normally
- Henoch-Schönlein purpura, a disease that causes small blood vessels in the body to become inflamed and leak
- hepatitis, inflammation of the liver caused by a virus
- human immunodeficiency virus (HIV), a virus that alters the immune system
- lupus, an autoimmune disease that occurs when the body attacks its own immune system
- malaria, a disease of the blood that is spread by mosquitos
- streptococcal infection, an infection that results when the bacteria that causes strep throat or a skin infection is left untreated

Other causes of secondary childhood nephrotic syndrome can include certain medications, such as aspirin, ibuprofen, or other nonsteroidal anti-inflammatory drugs, and exposure to chemicals, such as mercury and lithium.

Congenital Diseases and Childhood Nephrotic Syndrome

Congenital nephrotic syndrome is rare and affects infants in the first 3 months of life.[2] This type of nephrotic syndrome, sometimes called infantile nephrotic syndrome, can be caused by

- inherited genetic defects, which are problems passed from parent to child through genes
- infections at the time of birth

Read more about underlying diseases or infections that cause changes in kidney function in *Glomerular Diseases Overview* at *www.kidney.niddk.nih.gov*.

Which children are more likely to develop childhood nephrotic syndrome?

In cases of primary childhood nephrotic syndrome for which the cause is idiopathic, researchers are unable to pinpoint which children are more likely to develop the syndrome. However, as researchers continue to study the link between genetics and childhood nephrotic syndrome, it may be possible to predict the syndrome for some children.

Children are more likely to develop secondary childhood nephrotic syndrome if they

- have diseases that can damage their kidneys
- take certain medications
- develop certain types of infections

[2]Bakkaloglu SA, Schaefer F. Diseases of the kidney and urinary tract in children. In: Taal MW, Chertow GM, Marsden PA, et al., eds. *Brenner and Rector's The Kidney.* 9th ed. Philadelphia: Saunders; 2011: 2622–2643.

What are the signs and symptoms of childhood nephrotic syndrome?

The signs and symptoms of childhood nephrotic syndrome may include

- edema—swelling, most often in the legs, feet, or ankles and less often in the hands or face
- albuminuria—when a child's urine has high levels of albumin
- hypoalbuminemia—when a child's blood has low levels of albumin
- hyperlipidemia—when a child's blood cholesterol and fat levels are higher than normal

In addition, some children with nephrotic syndrome may have

- blood in their urine
- symptoms of infection, such as fever, lethargy, irritability, or abdominal pain
- loss of appetite
- diarrhea
- high blood pressure

What are the complications of childhood nephrotic syndrome?

The complications of childhood nephrotic syndrome may include

- **infection.** When the kidneys are damaged, a child is more likely to develop infections because the body loses proteins that normally protect against infection. Health care providers will prescribe medications to treat infections. Children with childhood nephrotic syndrome should receive the pneumococcal vaccine and yearly flu shots to prevent those infections. Children should also receive age-appropriate vaccinations, although a health care provider may delay certain live vaccines while a child is taking certain medications.
- **blood clots.** Blood clots can block the flow of blood and oxygen through a blood vessel anywhere in the body. A child is more likely to develop clots when he or she loses proteins through the urine. The health care provider will treat blood clots with blood-thinning medications.
- **high blood cholesterol.** When albumin leaks into the urine, the albumin levels in the blood drop. The liver makes more albumin to make up for the low levels in the blood. At the same time, the liver makes more cholesterol. Sometimes children may need treatment with medications to lower blood cholesterol levels.

How is childhood nephrotic syndrome diagnosed?

A health care provider diagnoses childhood nephrotic syndrome with

- a medical and family history
- a physical exam
- urine tests
- a blood test
- ultrasound of the kidney
- kidney biopsy

Medical and Family History

Taking a medical and family history is one of the first things a health care provider may do to help diagnose childhood nephrotic syndrome.

Physical Exam

A physical exam may help diagnose childhood nephrotic syndrome. During a physical exam, a health care provider most often

- examines a child's body
- taps on specific areas of the child's body

Urine Tests

A health care provider may order the following urine tests to help determine if a child has kidney damage from childhood nephrotic syndrome.

Dipstick test for albumin. A dipstick test performed on a urine sample can detect the presence of albumin in the urine, which could mean kidney damage. The child or a caretaker collects a urine sample in a special container. For the test, a nurse or technician places a strip of chemically treated paper, called a dipstick, into the child's urine sample. Patches on the dipstick change color when albumin is present in urine.

Urine albumin-to-creatinine ratio. A health care provider uses this measurement to estimate the amount of albumin passed into the urine over a 24-hour period. The child provides a urine sample during an appointment with the health care provider. Creatinine is a waste product filtered in the kidneys and passed in the urine. A high urine albumin-to-creatinine ratio indicates that the kidneys are leaking large amounts of albumin into the urine.

Blood Test

A blood test involves drawing blood at a health care provider's office or a commercial facility and sending the sample to a lab for analysis. The lab tests the sample to estimate how much blood the kidneys filter each minute, called the estimated glomerular filtration rate, or eGFR. The test results help the health care provider determine the amount of kidney damage. Health care providers may also order other blood tests to help determine the underlying disease that may be causing childhood nephrotic syndrome.

Ultrasound of the Kidney

Ultrasound uses a device, called a transducer, that bounces safe, painless sound waves off organs to create an image of their structure. A specially trained technician performs the procedure in a health care provider's office, an outpatient center, or a hospital. A radiologist—a doctor who specializes in medical imaging—interprets the images to see if the kidneys look normal; a child does not need anesthesia.

Kidney Biopsy

Biopsy is a procedure that involves taking a small piece of kidney tissue for examination with a microscope. A health care provider performs the biopsy in an outpatient center or a hospital. The health care provider will give the child light sedation and local anesthetic; however, in some cases, the child will require general anesthesia. A pathologist—a doctor who specializes in diagnosing diseases—examines the tissue in a lab. The test can help diagnose childhood nephrotic syndrome.

When the health care provider suspects a child has minimal change disease, he or she often starts treatment with medications without performing a biopsy. If the medication is effective, the child does not need a biopsy. In most cases, a health care provider does not perform a biopsy on children younger than age 12 unless he or she thinks that another disease is the cause.

How is childhood nephrotic syndrome treated?

Health care providers will decide how to treat childhood nephrotic syndrome based on the type:

- primary childhood nephrotic syndrome: medications
- secondary childhood nephrotic syndrome: treat the underlying illness or disease
- congenital nephrotic syndrome: medications, surgery to remove one or both kidneys, and transplantation

Primary Childhood Nephrotic Syndrome

Health care providers treat idiopathic childhood nephrotic syndrome with several types of medications that control the immune system, remove extra fluid, and lower blood pressure.

- **Control the immune system.** Corticosteroids are a group of medications that reduce the activity of the immune system, decrease the amount of albumin lost in the urine, and decrease swelling. Health care providers commonly use prednisone or a related corticosteroid to treat idiopathic childhood nephrotic syndrome. About 90 percent of children achieve remission with daily corticosteroids for 6 weeks and then a slightly smaller dose every other day for 6 weeks.[2] Remission is a period when the child is symptom-free.

  Many children relapse after initial therapy, and health care providers treat them with a shorter course of corticosteroids until the disease goes into remission again. Children may have multiple relapses; however, they most often recover without long-term kidney damage.

  When a child has frequent relapses or does not respond to treatment, a health care provider may prescribe other medications that reduce the activity of the immune system. These medications prevent the body from making antibodies that can damage kidney tissues. They include

  – cyclophosphamide
  – mycophenolate (CellCept, Myfortic)
  – cyclosporine
  – tacrolimus (Hecoria, Prograf)

  A health care provider may use these other immune system medications with corticosteroids or in place of corticosteroids.

- **Remove extra fluid.** A health care provider may prescribe a diuretic, a medication that helps the kidneys remove extra fluid from the blood. Removing the extra fluid can often help to lower blood pressure.
- **Lower blood pressure.** Some children with childhood nephrotic syndrome develop high blood pressure and may need to take additional medications to lower their blood pressure. Two types of blood pressure-lowering medications, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, have the additional benefit of slowing the progression of kidney disease. Many children with nephrotic syndrome require two or more medications to control their blood pressure.

Secondary Childhood Nephrotic Syndrome

Health care providers treat secondary childhood nephrotic syndrome by treating the underlying cause of the primary illness. For example, a health care provider may treat children by

- prescribing antibiotics for an infection
- adjusting medications to treat lupus, HIV, or diabetes
- changing or stopping medications that are known to cause secondary childhood nephrotic syndrome

While treating the underlying cause, the health care provider will also treat the child to improve or restore kidney function with the same medications used to treat primary childhood nephrotic syndrome.

Caretakers should make sure that children take all prescribed medications and follow the treatment plan recommended by their health care provider.

Read more about specific treatments for secondary childhood nephrotic syndrome in *Glomerular Diseases Overview* at *www.kidney.niddk.nih.gov*.

Congenital Nephrotic Syndrome

Researchers have found that medications are not effective in treating congenital nephrotic syndrome, and that most children will need a kidney transplant by the time they are 2 or 3 years old. A kidney transplant is surgery to place a healthy kidney from someone who has just died or a living donor, most often a family member, into a person's body to take over the job of the failing kidney. To keep the child healthy until the transplant, the health care provider may recommend the following:

- albumin injections to make up for the albumin lost in urine
- diuretics to help remove extra fluid that causes swelling
- antibiotics to treat the first signs of infection
- growth hormones to promote growth and help bones mature
- removal of one or both kidneys to decrease the loss of albumin in the urine
- dialysis to artificially filter wastes from the blood if the kidneys fail

Read more in *Treatment Methods for Kidney Failure in Children* at *www.kidney.niddk.nih.gov*.

How can childhood nephrotic syndrome be prevented?

Researchers have not found a way to prevent childhood nephrotic syndrome when the cause is idiopathic or congenital.

Eating, Diet, and Nutrition

Children who have nephrotic syndrome may need to make changes to their diet, such as

- limiting the amount of sodium, often from salt, they take in each day
- reducing the amount of liquids they drink each day
- eating a diet low in saturated fat and cholesterol to help control elevated cholesterol levels

Parents or caretakers should talk with the child's health care provider before making any changes to the child's diet.

Read more in *Nutrition for Chronic Kidney Disease in Children* at *www.kidney.niddk.nih.gov*.

Points to Remember

- Childhood nephrotic syndrome is not a disease in itself; rather, it is a group of symptoms that
  - indicate kidney damage—particularly damage to the glomeruli, the tiny units within the kidney where blood is filtered
  - result in the release of too much protein from the body into the urine
- The two types of childhood nephrotic syndrome are
  - primary—the most common type of childhood nephrotic syndrome, which begins in the kidneys and affects only the kidneys
  - secondary—the syndrome is caused by other diseases
- The signs and symptoms of childhood nephrotic syndrome may include
  - edema—swelling, most often in the legs, feet, or ankles and less often in the hands or face
  - albuminuria—when a child's urine has high levels of albumin
  - hypoalbuminemia—when a child's blood has low levels of albumin
  - hyperlipidemia—when a child's blood cholesterol and fat levels are higher than normal
- A health care provider may order urine tests to help determine if a child has kidney damage from childhood nephrotic syndrome.
- Health care providers will decide how to treat childhood nephrotic syndrome based on the type:
  - primary childhood nephrotic syndrome: medications
  - secondary childhood nephrotic syndrome: treat the underlying illness or disease
  - congenital nephrotic syndrome: medications, surgery to remove one or both kidneys, or transplantation

Hope through Research

In recent years, researchers have learned much about kidney disease. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) sponsors many programs aimed at understanding the causes and developing treatments for childhood nephrotic syndrome.

The Nephrotic Syndrome Study Network (NEPTUNE), funded under National Institutes of Health (NIH) clinical trial number NCT01240564, is a network of researchers studying why this kidney disease happens. The researchers collect kidney tissue and other samples, such as blood and urine, from children and adults scheduled to have a kidney biopsy. Researchers will use the samples to better understand the development and progression of focal segmental glomerulosclerosis, minimal change disease, and membranous nephropathy.

Immune System Related Kidney Disease, funded under NIH clinical trial number NCT00001979, studies kidney diseases related to the immune system, including nephrotic syndrome, in children 5 years of age and older and adults. A study of kidney disease biomarkers, funded under NIH clinical trial number NCT00255398, identifies biomarkers that may help scientists predict what kidney disease a person has and whether a given person would respond to particular therapies. Biomarkers are identified in blood and urine samples from children with idiopathic nephrotic syndrome or glomerular disease and adults with certain glomerular diseases.

Clinical trials are research studies involving people. Clinical trials look at safe and effective new ways to prevent, detect, or treat disease. Researchers also use clinical trials to look at other aspects of care, such as improving the quality of life for people with chronic illnesses. To learn more about clinical trials, why they matter, and how to participate, visit the NIH Clinical Research Trials and You website at *www.nih.gov/health/clinicaltrials*. For information about current studies, visit *www.ClinicalTrials.gov*.

For More Information

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Internet: www.kidneyfund.org

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Email: info@aspneph.com
Internet: www.aspneph.com

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Fax: 856–439–9982
Email: info@myAST.org
Internet: www.myast.org

Life Options
c/o Medical Education Institute, Inc.
414 D'Onofrio Drive, Suite 200
Madison, WI 53719
Phone: 1–800–468–7777 or 608–833–8033
Fax: 608–833–8366
Internet: www.lifeoptions.org
www.kidneyschool.org

National Kidney Foundation
30 East 33rd Street
New York, NY 10016–5337
Phone: 1–800–622–9010 or 212–889–2210
Fax: 212–689–9261
Internet: www.kidney.org

United Network for Organ Sharing
P.O. Box 2484
Richmond, VA 23218
Phone: 1–888–894–6361 or 804–782–4800
Fax: 804–782–4817
Internet: www.unos.org

Resources

American Society of Transplantation
Facts About Kidney Transplantation: Pediatric Patient Education Brochure
www.myast.org/sites/default/files/images/2_FACT%20ABOUT%20KIDNEYTRANSPLANTATION%20%20FINAL.pdf

National Kidney Foundation
Children with Chronic Kidney Disease: Tips for Parents
www.kidney.org/atoz/content/childckdtips.cfm

Family Focus newsletter
www.kidney.org/patients/pfc/backissues.cfm

Employers' Guide
www.kidney.org/atoz/content/employersguide.cfm

Nemours KidsHealth Website
When Your Child Has a Chronic Kidney Disease
www.kidshealth.org/parent/medical/kidney/chronic_kidney_disease.html

What's the Deal With Dialysis?
www.kidshealth.org/kid/feel_better/things/dialysis.html

Nephkids
Cyber-support group
www.cybernephrology.ualberta.ca/nephkids

United Network for Organ Sharing
Organ Transplants: What Every Kid Needs to Know
www.unos.org/docs/WEKNTK.pdf

U.S. Department of Health and Human Services, Centers for Medicare & Medicaid Services
Medicare Coverage of Kidney Dialysis & Kidney Transplant Services
www.medicare.gov/Publications/Pubs/pdf/10128.pdf

U.S. Social Security Administration
Benefits For Children With Disabilities
www.socialsecurity.gov/pubs/EN-05-10026.pdf

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The National Kidney Disease Education Program (NKDEP) is an initiative of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, U.S. Department of Health and Human Services. The NKDEP aims to raise awareness of the seriousness of kidney disease, the importance of testing those at high risk, and the availability of treatment to prevent or slow kidney disease.

You may also find additional information about this topic by visiting MedlinePlus at *www.medlineplus.gov*.

This publication may contain information about medications and, when taken as prescribed, the conditions they treat. When prepared, this publication included the most current information available. For updates or for questions about any medications, contact the U.S. Food and Drug Administration toll-free at 1–888–INFO–FDA (1–888–463–6332) or visit *www.fda.gov*. Consult your health care provider for more information.

National Kidney and Urologic Diseases Information Clearinghouse

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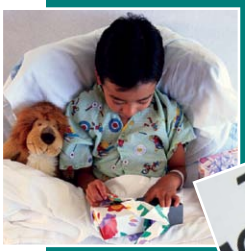
The National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health of the U.S. Department of Health and Human Services. Established in 1987, the Clearinghouse provides information about diseases of the kidneys and urologic system to people with kidney and urologic disorders and to their families, health care professionals, and the public. The NKUDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about kidney and urologic diseases.

This publication is available at *www.kidney.niddk.nih.gov*.









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